



CLCN5 gene

chloride voltage-gated channel 5

Normal Function

The *CLCN5* gene provides instructions for making a protein called CIC-5 that transports charged atoms (ions) across cell membranes. Specifically, CIC-5 exchanges negatively charged atoms of chlorine (chloride ions) for positively charged atoms of hydrogen (protons or hydrogen ions). Based on this function, CIC-5 is known as a H^+/Cl^- exchanger.

CIC-5 is found primarily in the kidneys, particularly in structures called proximal tubules. These structures help to reabsorb nutrients, water, and other materials that have been filtered from the bloodstream. The kidneys reabsorb needed materials into the blood and excrete everything else into the urine.

Within proximal tubule cells, CIC-5 is embedded in specialized compartments called endosomes. Endosomes are formed at the cell surface to carry proteins and other molecules to their destinations within the cell. CIC-5 transports hydrogen ions into endosomes and chloride ions out, which helps these compartments maintain the proper acidity level (pH). Endosomal pH levels must be tightly regulated for proximal tubule cells to function properly.

Health Conditions Related to Genetic Changes

Dent disease

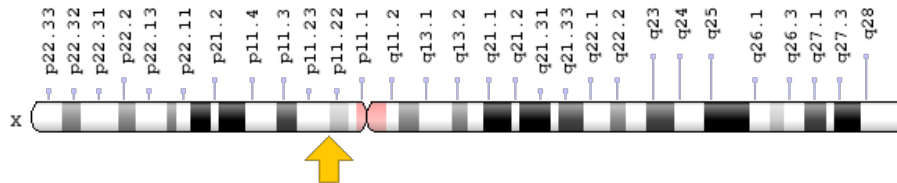
About 150 mutations in the *CLCN5* gene have been found to cause Dent disease 1, a chronic kidney disorder that can cause kidney failure. Most of the mutations lead to the production of an abnormally short, nonfunctional version of CIC-5 or prevent cells from producing any of this protein. A loss of CIC-5 alters the regulation of endosomal pH, which disrupts the overall function of proximal tubule cells and prevents them from reabsorbing proteins and other materials into the bloodstream. As a result, proteins are lost through the urine (tubular proteinuria). A failure to reabsorb calcium and other nutrients into the bloodstream can cause bone defects, kidney stones, and related health problems in people with Dent disease 1. Abnormal proximal tubule function ultimately leads to kidney failure in most affected individuals.

hereditary hypophosphatemic rickets

Chromosomal Location

Cytogenetic Location: Xp11.23, which is the short (p) arm of the X chromosome at position 11.23

Molecular Location: base pairs 49,922,615 to 50,099,235 on the X chromosome (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- chloride channel 5
- chloride channel protein 5
- chloride channel, voltage-sensitive 5
- chloride transporter CIC-5
- cIC-5
- CLC5
- CLCK2
- CLCN5_HUMAN
- DENTS
- H(+)/Cl(-) exchange transporter 5
- hCIC-K2
- hCIC-K2
- NPHL1
- NPHL2
- XLRH
- XRN

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Transport into the Cell from the Plasma Membrane: Endocytosis
<https://www.ncbi.nlm.nih.gov/books/NBK26870/>
- National Institute of Diabetes and Digestive and Kidney Diseases: The Kidneys and How They Work
<https://www.niddk.nih.gov/health-information/kidney-disease/kidneys-how-they-work>
- Neuromuscular Disease Center, Washington University: Chloride channels
<http://neuromuscular.wustl.edu/mother/chan.html#CLC1>

GeneReviews

- Dent Disease
<https://www.ncbi.nlm.nih.gov/books/NBK99494>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CLCN5%5BTIAB%5D%29+OR+%28CLC-5%5BTIAB%5D%29+OR+%28CLC5%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- CHLORIDE CHANNEL 5
<http://omim.org/entry/300008>

Research Resources

- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=CLCN5%5Bgene%5D>
- HGNC Gene Family: Chloride voltage-gated channels
<http://www.genenames.org/cgi-bin/genefamilies/set/302>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=2023

- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/1184>
- UniProt
<http://www.uniprot.org/uniprot/P51795>

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Reviewed: September 2012

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
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Department of Health & Human Services